

## Case Report

# Imatinib mesylate induced lichenoid drug eruption masquerading as small plaque parapsoriasis

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### ABSTRACT

Imatinib mesylate (IM) is a tyrosine kinase inhibitor approved for chronic myeloid leukemia, gastrointestinal stromal tumor and few dermatological conditions such as dermatofibrosarcoma protruberans, systemic sclerosis and systemic mastocytosis among other conditions. It is known to cause non lichenoid eruptions commonly and rarely it can cause lichenoid drug eruption. Small plaque parapsoriasis is a monoclonal T cell disorder with clinical similarity to psoriasis characterised by small sized plaques with digitate appearance. We report a case of 75 year old male on IM for gastrointestinal stromal tumor who presented with clinical features suggestive of small plaque parapsoriasis which was eventually proved as lichenoid drug eruption secondary to IM on biopsy. IM was identified as the offending drug and the eruptions subsided one month after discontinuation of the drug.

**Keywords:** Imatinib mesylate, Lichenoid drug eruption, Small plaque parapsoriasis, Gastrointestinal stromal tumor

### INTRODUCTION

Imatinib mesylate (Gleevec™, STI571) is a selective inhibitor of BCR-ABL, c-kit and platelet-derived factor receptor (PDGFR). It has been approved for various dermatological conditions such as dermatofibrosarcoma protruberans, scleroderma graft versus host disease, systemic sclerosis, systemic mastocytosis and melanoma with c kit mutations and several systemic conditions such as unresectable gastrointestinal stromal tumors, chronic myeloid leukemia, myelodysplastic syndromes with PDGFR reordering, hypereosinophilic syndromes and chronic eosinophilic leukemia. Cutaneous adverse effects associated with imatinib mesylate commonly include maculopapular eruptions, psoriasiform lesions, acute generalised exanthematous pustulosis and Steven Johnson syndrome.<sup>1</sup> These non lichenoid reactions are common and are well documented in the literature.

Lichenoid drug reactions secondary to this drug are unusual and have rarely been reported.<sup>2</sup> Small plaque parapsoriasis is characterised by well circumscribed plaques of sizes two to six centimetres in diameter located on the trunk without atrophy or poikiloderma.<sup>3</sup> This case has been reported for the atypical presentation of lichenoid drug eruptions, masquerading as the lesions of small plaque parapsoriasis and also lichenoid drug eruption secondary to imatinib mesylate which is a rare entity.

### CASE REPORT

A 75 year old male patient presented with multiple asymptomatic lesions on the neck, trunk and extremities of more than two months duration. Patient is a known case of gastrointestinal stromal tumor on imatinib mesylate at a dosage of 400 mg/day for the past four months. There is no history of previous episodes of

similar lesions, no history of dental amalgams or any other drug intake.



**Figure 1: Numerous hypopigmented patches on the anterior surface of the trunk.**

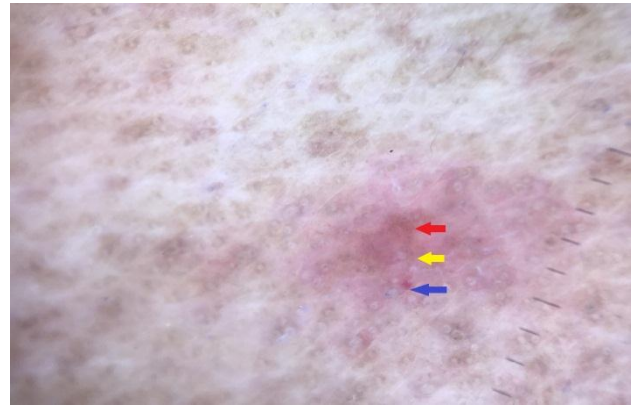


**Figure 2: Multiple hypo and hyperpigmented patches on the sides of the trunk.**

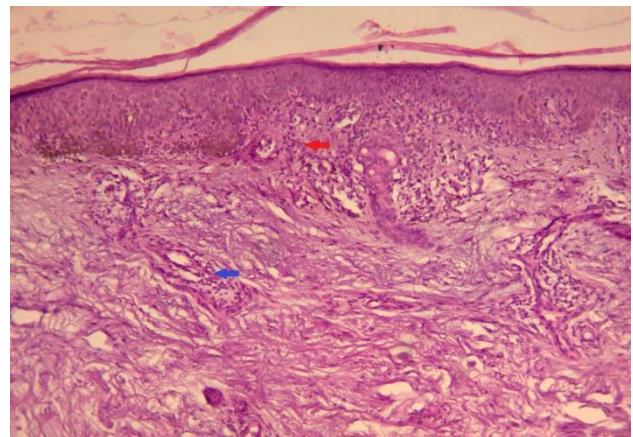
On examination multiple round to oval shaped, scaly hypo and hyperpigmented patches and plaques of two to three cm in diameter, located over the neck, anterior and posterior sides of the trunk (Figure 1 and 2), flexural and extensor aspect of arm and forearms, extensor surface of the legs and the dorsum of both feet. Oral cavity examination was normal with caries teeth of the last two molars. Rest of the mucosal examination including buccal and genital mucosa was normal. Examination of other sites including nails, hair, palms and soles was normal.

Based on the history and clinical examination, small plaque parapsoriasis, pityriasis rosea and secondary syphilis were considered as other differential diagnosis.

All routine laboratory investigations were within normal limits, special investigations such as VDRL and ELISA were non-reactive. Dermoscopic examination of the plaque on the trunk revealed a pink brown background with brown to red globules with scaling and absence of Wickham's striae (Figure 3) indicating lichenoid drug eruption as a probable diagnosis. Skin biopsy revealed irregular acanthosis with elongated rete ridges with upper dermis having band like infiltrates of lymphocytes, histiocytes and pigment laden macrophages with perivascular and periadnexal inflammatory cell infiltrates (Figure 4). These features were consistent with that of lichenoid drug eruption.



**Figure 3: Red arrow indicates brown dots; yellow arrow indicates lack of starburst pattern indicates absence of Wickham's striae; blue arrow indicates red globules.**



**Figure 4: H&E (10X); red arrow indicates dense lymphocytic infiltrates obscuring the dermoepidermal junction; blue arrow indicates indicates perivascular lymphocytic infiltrates.**

## DISCUSSION

Imatinib mesylate is a tyrosine kinase inhibitor. It inhibits the fusion product BCR-ABL which acts through the tyrosine kinase pathway to cause proliferation of leukemic cells in chronic myelogenous leukemia. Imatinib also inhibits c-kit and platelet-derived growth

factor (PDGF) which acts through the tyrosine kinase pathway. Since the c-kit receptor is implicated as the causative factor in the pathogenesis of dermatofibrosarcoma protuberans, gastrointestinal stromal tumor, systemic sclerosis and systemic mastocytosis hence IM is indicated at doses of 400 to 600 mg/day in CML, GIST, dermatofibrosarcoma protuberans, systemic mastocytosis and a low dose of 200 mg/day in systemic sclerosis.<sup>1,4</sup>

Imatinib induced cutaneous adverse effects include macular-papular eruption, superficial edema, pigmentary disorders, hypopigmentation or depigmentation, hyperpigmentation, psoriasis and psoriasiform eruption, pityriasis rosea-like eruption, acute generalized exanthematous pustulosis, Stevens-Johnson syndrome, urticaria, neutrophilic dermatosis, photosensitivity, porphyria and pseudoporphyria but rarely lichenoid reactions.<sup>1</sup>

Patient developed cutaneous eruptions two months after starting of IM of 400 mg/day for GIST which can occur in patients on IM. The time interval ranges from one month to fifteen months for the appearance of cutaneous adverse effects after initiation of IM therapy which was consistent in the present case.<sup>5</sup> Imatinib mesylate was identified as the offending drug and was withdrawn for one month after which the eruption subsided with persistent hyperpigmentation. This was similar to an isolated case report of imatinib induced extensive hyperpigmentation in chronic myeloid leukemia.<sup>6</sup> Till date very few cases of IM-associated lichenoid drug eruption have been described over the last decade.<sup>5</sup>

Lichenoid drug eruption (LDE) is an interface dermatitis caused by ingestion, contact or inhalation of a variety of drugs and has a latent period ranging from several weeks to months after onset of drug intake. LDE have been reported to a wide variety of drugs. These may commonly include, angiotensin converting enzyme inhibitors, thiazide diuretics, gold, antimalarials, penicillamine, nonsteroidal antiinflammatory agents, dental amalgams, sulfasalazine,  $\beta$  blockers, and proton pump inhibitors.<sup>5</sup> Similar to present case, lichenoid drug eruption commonly manifests as skin lesions comprising papules or plaques, usually on the photo exposed parts of the skin and often spares the oral mucosa, genitalia and typically lack Wickham's striae.<sup>5</sup> Patients with LDE are often taking more than one drug hence making the diagnosis challenging. Resolution of lesions on discontinuation of the offending drug favours the diagnosis of LDE as seen in the present case where in which regression of the

lesions were seen after the withdrawal of imatinib mesylate.<sup>5</sup>

The lichenoid drug eruption was managed conservatively by topical emollients and steroids and advised the patient to continue with imatinib mesylate.

## CONCLUSION

Lichenoid drug eruption secondary to imatinib mesylate increases the spectrum of lichenoid rash, which also highlights on differentiating it from psoriasiform dermatitis. Early diagnosis of the morphological pattern of such drug eruption is crucial to prevent the subsequent discontinuation of imatinib mesylate, which has drastically changed the treatment and prognosis of chronic myeloid leukemia and gastrointestinal stromal tumor. Once identified, lichenoid drug eruption can be managed conservatively.

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